THE PRESENT STATUS AND FUTURE OF PARASITOLOGY

SUMMARY REPORT OF A CONFERENCE

Corrected

October 20-22, 1980

Parasites directly affect the health and well-being of three-quarters of mankind. They are intimately linked to medicine in the developing countries where some 3 billion people live on the edge of existence; health in those countries is also interlocked with nutrition and soaring population rates. While parasitic diseases in the third world are largely unknown to Americans, the high prevalence of worms and protozoa in their fellow countrymen also receives little attention. As many as 50 million Americans are said to be infected with helminths, and 36% of the population of the United States has had toxoplasmosis. The incidence of all parasitic diseases accelerates as both tourism and the flow of immigrants expand, legal and illegal, carrying parasites such as the malarias and schistosomes. Parasitic diseases are as well the most economically important group of animal diseases worldwide, producing estimated global losses of over $250 billion a year in livestock production.

Unfortunately, schools of medicine, veterinary medicine and public health throughout the developed and developing world continue to neglect this critical field which is too often deemed to reflect unimportant diseases of poor rural people. For many years the conquest of parasitic diseases led by campaigns against hookworm and malaria represented a paramount interest of The Rockefeller Foundation and its International Health Division. The Division of Agricultural Sciences has spearheaded an international effort addressing hemoparasitic diseases of livestock

including trypanosomiasis, East Coast Fever, babesiosis and anaplasmosis. More recently the Foundation opened a frontal attack on schistosomiasis which expanded to a program in the 'Great Neglected' Diseases.

Some months ago, representatives of The Rockefeller and the Josiah Macy, Jr., Foundations decided to join forces in a conference to evaluate the current situation in American parasitology and to determine future steps needed to strengthen the field. The participants were drawn from schools of medicine, public health and veterinary medicine and biology departments of colleges, biomedical research institutes, federal health agencies and philanthropic organizations.

Academic Status: Parasitology has become an isolated field, both scientifically and geographically. It is not considered an essential component of most curricula nor is it accepted as an integral unit of basic science and clinical departments. Parasitology is a core course in all veterinary schools, but the quality and quantity of the content varies from university to university. Schools of Public Health which have traditionally been concerned with parasitology are retreating. Furthermore, there is no modern textbook concerned with process and scientific principles.

Graduate training in parasitology suffers from a lack of recognition, of career opportunities and of fellowship support at both predoctoral and postdoctoral levels. A 1978 survey of graduate training programs revealed an overemphasis on such traditional disciplines as taxonomy, life-cycles and morphology, while genetics, biochemistry, immunology, epidemiology, and molecular biology did not receive appropriate stress.

Although parasites are the number one source of diseases in animals, veterinary schools and departments of veterinary science are also derelict in undergraduate and graduate training. While the curricula are integrated, parasitology's ties with other disciplines are insufficient. Both instruction and research are handicapped by a shortage of faculty members with specialized training in modern biomedical science.

Scientific Interface: Research in parasitology should place greater emphasis on its chemical and molecular base - immunoparasitology, molecular biology and biochemistry. The conferees repeatedly commented on the importance of interdisciplinary confluences linking parasitology with immunology, genetics and biochemistry. Such interplay would afford investigators maximum freedom of choice for their research endeavors.

For a number of years physiology was the scientific base of pharmacology, but more recently the pendulum has swung to a biochemical relationship. The biochemical properties of parasites and the need for more effective therapeutic drugs open excellent opportunities for pharmacological/biochemical studies. As one participant whose research is in that field, commented, too many of the available drugs have 'horrendous' side effects. Biological and chemical principles have not been adequately applied in pharmacological developments.

Paul Ehrlich's development of arsenical compounds related to salvarsan, which had limited power to kill trypanosomes, probably marked the beginning of drug therapy for parasitic diseases. The question was raised, why have so few effective derivatives of tryparsamide for the treatment of parasitic disease been developed in the past forty years? Why has no drug been developed for the effective treatment of filariasis or Chagas'

disease? The answer relates in part to economics with the cost of development of a drug estimated to be many millions of dollars. Furthermore, drug development has been taken over by the pharmaceutical manufacturers. They are reluctant to make large investments for drugs designed primarily for the third world where financial returns would be limited.

In January 1979, the National Academy of Sciences sponsored a conference on drug development for the third world. This resulted in the creation of a task-force to investigate the problems and opportunities, and the drug industry is reported to be taking steps to enhance its role in the field.

The recently established Center for Public Resources is creating a non-profit firm, The Drug and Vaccine Development Corporation, to assist scientists in patenting and licensing their new drugs for the treatment of parasitic diseases. The U.S. Army's Walter Reed Institute of Medical Research has been successful with drug development for military units while N.I.H. invested $16 million in research on parasitology and medical entomology. The World Health Organization encourages the development of drugs for use in the third world.

New Frontiers: As an example of opportunities in the interrelationship between parasitology, biochemistry, immunology and pharmacology, a member of a department of medicine described his studies on the ability of phagocytic cells in the human body to produce toxic agents as part of the immune response. The oxygen-peroxidase killing systems in eosinophils and neutrophils liberate highly toxic pharmacological agents which are delivered precisely to the parasites.

While research on immunological aspects of bacterial and viral diseases advanced rapidly, the host-parasite relationship in immunology did not receive comparable attention until the past few years. Investigations of schistosomiasis at the cellular and molecular levels have shown that immunopathology is due to an immunological reaction of the delayed hypersensitivity type. Studies both *in vivo* and especially *in vitro* have identified the central role of the eosinophil in the defense of the host. Immunological research on Chagas' disease which is caused by *Trypansoma cruzi* showed that cell-mediated rather than humoral responses were the controlling factors in parasite/cell interactions.

Ecological studies in parasitology should relate directly to population dynamics. Such factors as 'susceptibility,' 'infected,' and 'immune' must be considered in regard to population reactions to parasitic microorganisms. In addition, environmental studies must distinguish between the period of invasion by a parasite and the onset of full-blown disease. More generally, there is need for better understanding of the biological factors determining whether or not a given parasite will be maintained in a population. In the absence of such understanding, vaccination programs will be at best, hit or miss.

Validation of the centrality of molecular biology in parasitic studies was verified by research on immunity and membranes in malarial sporozoites. A single antigen in the membrane was probably the basis of the immune reaction eliciting species and stage specific antibodies.

Immunology is only one aspect of the broad subject of parasitism, the physiological interrelations between parasites and their host. Parasitism provides biologists with remarkable examples of differentiation triggered by external factors and of biochemical adaptations between organisms of different kinds. *In vitro* cultivation of the

parasites apart from their hosts furnishes a powerful tool for dissecting the host-parasite relationship.

An example of the interaction between basic biomedical sciences and parasitology is the new summer course entitled The Biology of Parasitism, with an emphasis on immunology, molecular biology and biochemistry, held at the Marine Biological Laboratory, Woods Hole in 1980. Supported by the Edna McConnell Clark and Rockefeller Foundations, it was of wide popularity.

Financial Status: Sources of financial support continue to be too limited for the proper and expedient advancement of parasitology. The total sums allotted in N.I.H. research budgets declined between 1979 and 1980 and will probably continue to do so. Research support from the National Institute of Allergy and Infectious Diseases is placing special emphasis on the immunology of parasitic infections and the biological regulation of vectors.

Other sources include the U.S. Army whose support focuses on four diseases -- malaria, schistosomiasis, trypanosomiasis, and leishmaniasis. The U.S. Department of Agriculture has selected for research assistance parasitic diseases in beef and dairy cattle, swine, poultry and sheep with expenditures approximating 7 million dollars. Seven European-based drug companies spend 22 million dollars annually for parasitic studies. The World Health Organization's tropical diseases program concentrates on malaria, filariasis, leishmaniasis, trypanosomiasis and schistosomiasis. Only two American philanthropies, Edna McConnell Clark and Rockefeller are active in this field and their total expenditures are limited to 4.7 million dollars annually. Other health-related foundations would find tropical medicine and parasitology challenging and intriguing fields. Unfortunately, tropical medicine today

is viewed as a pejorative term because of previous neglect in terms of financing and interest by the scientific establishment.

A Forward Look: A consideration of the future of parasitology acknowledges the mounting interest in immunological, biochemical and molecular biological links as inciting a new wave for this neglected field. Parasitology has suffered from the absence of stirring new advances which could compare with the dramatic penicillin and streptomycin stories of the 1940s. Yet parasitology offers comparable opportunities for life-saving discoveries and diverse resources must be mobilized to inspire such initiatives. Malaria ranks as the king of diseases today with an estimated 300,000,000 cases and 1,000,000 deaths among children of Africa annually.

There are remarkable opportunities to apply molecular biology to parasitology. The conference showed that parasitology is at a critical point due to its limited role in education and research, its short supply of qualified scientists and its need for working relations with other disciplines. There is no question as to the overriding importance of the field and the challenging opportunities it offers. Increased financial support is imperative for the advancement of parasitology to its proper status in the world of biomedical science and the alleviation of the 'Great Neglected Diseases' of the world.